IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of	:	**Confirmation No. 1112**
Edwin SOUTHERN	:	Attorney Docket No. 2004_0200
Serial No. 10/772,467	:	Group Art Unit 1631
Filed February 6, 2004	:	Examiner Anna Skibinsky
ANALYZING POLYNUCLEOTIDE SEQUENCES	:	**Mail Stop: Appeal Brief- Patents**

REPLY BRIEF UNDER 37 C.F.R. § 41.41

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is responsive to the Examiner's Answer dated January 6, 2009 and further to the Appeal Brief of September 25, 2008.

A Request for Oral Hearing under 37 C.F.R. § 41.47 is submitted concurrently herewith with the required fee set forth in 37 C.F.R. § 41.20(b)(3).

The following is Appellant's Reply Brief, submitted under the provisions of 37 C.F.R. § 41.41.

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The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975.

REMARKS

Appellants herein provide the following remarks:

For items (1) to (8) and (11) in the Examiner's Answer Appellant has no comments.

For item (9) in the Examiner's Answer Appellant notes the following:

- 9.2: Appellant disagrees with the examiner's interpretation of the term *"predetermined"*. This term has a specific meaning, as outlined on page 14 of the Appeal Brief.

- 9.2: In relation to the *"oligonucleotides ... attached to the porous material"* feature of claims 17 and 86, the examiner cites col. 5, line 58 to col. 6, line 4 of Stavrianopoulos. In the cited passage, however, Stavrianopoulos is explicitly referring to solution-phase oligonucleotide probes rather than to immobilised oligonucleotides. This passage refers to *"fixed single-stranded analytes"* (col. 5, line 59) and it is this fixed material which corresponds to the immobilised oligonucleotides of present claims 17 and 86.

- 9.4: The examiner argues that Stavrianopoulos *"teaches in situ techniques (col. 5, lines 41-46) for attaching the nucleotide sequence"*. As explained on page 21 of the Appeal Brief, although the term "in situ" is indeed used by Stavrianopoulos in the cited passage, this term alone does not meet the requirements of claim 25. Claim 25 requires that *"the oligonucleotides are synthesized in situ"*, whereas Stavrianopoulos merely teaches that a whole cell may be fixed to a support. Stavrianopoulos does not disclose any oligonucleotide synthesis and *a fortiori* does not disclose any such synthesis *in situ* as required by claim 25.

For item (10) Appellant notes the following:

- Section 10 begins with a summary of Appellant's position from the examiner. This summary is incomplete as it focuses solely on one aspect of Appellant's argument. Section VII of the Appeal Brief included three separate points in relation to claim 17 (sub-headings A, B & C in the Appeal Brief) and made separate points in relation to the additional features of dependent claims 22, 23, 24 and 25 (and *mutatis mutandis* for claims 86 & 87). Although these points are picked up in the passages which follow the examiner's summary, they are ignored in the summary itself. Thus the opening passage of section 10 is misleading because it ignores the different strands of Appelant's

argument and instead presents our appeal as resting solely on the issue of whether Stavrianopoulos and Matkovich are "analogous art".

- The examiner argues that Stavrianopoulos and Matkovich are analogous art because they are both in *"the field of attaching macromolecules to a substrate"*. Appellant disagrees. Although it is inherent to both Stavrianopoulos and Matkovich that a macromolecule must be attached to a substrate, this does not mean that this is "the field" of the two documents. As mentioned in the Appeal Brief, Stavrianopoulos deals with nucleic acid assays whereas Matkovich is explicitly concerned with antibody (*i.e.* protein-based) assays *e.g.* see the Background section of Matkovich, culminating with the statement: *"Accordingly, there remains a need for improvements in multiwell plates to provide for increased antibody binding ..."*. The examiner has latched on to the stray mention of nucleic acids in column 6 of Matkovich in a document which otherwise focuses solely on protein binding, but this isolated phrase fails to transform "the field" of Matkovich in the manner suggested by the examiner.

- The examiner argues that the term "various" used by Stavrianopoulos (col. 8, line 43) *"is reasonably interpreted as being different oligonucleotides"*. On the contrary, this interpretation is not "reasonable". One reasonable way of using the Stavrianopoulos assay in a multiwell format would be to add the same analyte to separate wells and then to add a different probe to each well. Thus each well reveals whether a particular sequence is present in a single analyte. For instance, a single patient's blood could be screened for a dozen different mutations. In this format there are "various denatured analytes" but each analyte is identical, whereas claim 17 requires that *"the sequence of the oligonucleotides of a first cell is different from the sequence of the oligonucleotides of a second cell"*.

  The examiner argues that *"the DNA of the Stavrianopoulos et al. invention is taken from different samples such as lambda DNA (column 9, line 51) or adenovirus DNA (column 11, line 21). Therefore Stavrianopoulos et al. fairly teaches at least two different sequences."* The two cited types of DNA sample are disclosed in separate examples – example 3 (lambda DNA) and example 5 (adenovirus DNA). There is no disclosure that these two samples should be attached to the same support in a single experiment. The examiner's argument merely confirms that Stavrianopoulos never suggested that different sequences might be attached to a single support, as required by claims 17 and 86.

- The examiner has failed to show where either Stavrianopoulos or Matkovich discloses or suggests the final feature of claim 17, namely to provide an assay in which the nucleic acids attached to the support *"are shorter than the polynucleotide"* analyte.

- The examiner's capitalisation of the word "explicitly" on page 13 of the Examiner's Answer is presumably an attempt to suggest that the silane linker used by Stavrianopoulos was useful for covalent attachment of DNA. On the contrary, however, pages 17-19 of the Appeal Brief explain in detail that the silane used by Stavrianopoulos was specifically and deliberately used to facilitate non-covalent binding of DNA. Lines 32-35 of col. 8 confirms that the silane binds to *"negatively charged"* molecules *i.e.* via ionic bonding, not covalent bonding. The examiner notes that Matkovich mentions the possibility of using covalent attachment as one possibility, but fails to explain why a person starting with ionic attachment of an ionic molecule (DNA) in Stavrianopoulos would instead choose to use covalent attachment when adding the porous layer of Matkovich.

- In section E on page 14 the examiner admits that Stavrianopoulos *"does not explicitly teach attachment via a terminal nucleotide"*, as required by claim 24, but argues that the Stavrianopoulos disclosure *"encompasses"* such attachment. The relevant issue is not whether terminal attachment is "encompassed", however, but whether this specific feature is taught by Stavrianopoulos or by Matkovich. The examiner is correct that the immobilized nucleotides in Stavrianopoulos should be able to hybridize, but this does not imply terminal attachment. On the contrary, as explained in the Appeal Brief, standard covalent attachment of nucleic acids to porous membranes, while retaining the ability to hybridize, occurs via internal thymidine residues rather than *"by a terminal nucleotide"*.

- In section F on page 14 the examiner argues that Stavrianopoulos teaches techniques *"wherein the oligonucleotide exists 'in situ' within the cell."* In claim 25, however, the relevant feature is not merely that an oligonucleotide "exists" *in situ*, but rather that it is synthesized *in situ*. Stavrianopoulos does not disclose any oligonucleotide synthesis and *a fortiori* does not disclose any such synthesis *in situ* as required by claim 25.

Appellant's failure to comment on any particular point in this Reply does not indicate that the examiner's position is correct.

CONCLUSION

In view of the foregoing as well as in view of the Appeal Brief of September 25, 2008, it is respectfully submitted that the rejection of claims 17-27 and 86-87 is untenable and should be reversed.

Respectfully submitted,

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